

### **REMARKS**

The specification has been amended to delete reference to U.S. Patent Application Nos. 09/369,941, 60/128,608, and 60/095,913, to which priority is no longer claimed in this application.

Claims 31, 33-38, 40 and 44 were pending prior to the amendments made herein. Claims 45 and 46 have been added. Thus, upon entry of the above amendments, claims 31, 33-38, 40, 44-46 will be pending. Claim 31 has been amended to clarify Applicant's claimed invention. Support for the amendment to claim 31 can be found, *e.g.*, at page 6, lines 7-9; page 17, lines 15-16; and page 23, lines 15-17. Claims 45 and 46 are supported by the present specification, *e.g.*, at page 21, lines 1-4.

No new matter has been introduced by the present amendments.

### **THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH SHOULD BE WITHDRAWN**

Claims 31, 33-38, 40 and 44 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Specifically, the Examiner alleges that the claims are incomplete for omitting an essential step(s) of how to determine cancer is treated. In particular, the Examiner states that "while it is not necessary to recite the exact method steps of treating cancer, the method is not considered complete if the method steps do not refer back to the preamble 'a method of treating cancer.'"

In response, and without agreeing with the Examiner's rejection, Applicant has amended claim 31 so that the method steps refer back to the preamble.

In view of the foregoing, Applicant submits that the rejection under 35 U.S.C. §112, second paragraph, has been obviated and should be withdrawn.

**THE REJECTION UNDER 35 U.S.C. § 112,  
FIRST PARAGRAPH, SHOULD BE WITHDRAWN**

Claims 31, 33-38, 40 and 44 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner contends that the claims contain subject matter which are not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. In particular, the Examiner contends that the specification fails to teach a method of treating a single type of cancer by using *Quillaja saponaria* saponin or any of its chemically modified forms either *in vivo* or *in vitro*, and the specification fails to provide any working example that demonstrates the effectiveness of *Quillaja saponaria* saponin in treating cancer. The Examiner further alleges that in view of the limited teaching in the specification and unpredictability in the art, one skilled in the art would have to engage in undue experimentation to practice the method as claimed. Applicant respectfully disagrees, and submits that the claims, as amended, are fully enabled by the specification as described in detail below.

**THE LEGAL STANDARD FOR ENABLEMENT**

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and

the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Working examples are not necessary to meet the enablement requirement and the lack of examples should not be equated with lack of direction. "Nothing more than objective enablement is required, and therefore it is irrelevant whether the teaching is provided through broad terminology or illustrative examples." *In re Marzocchi*, 439 F 2d 220.

The law also does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims. *See In re Fisher*, 166 USPQ 18, 24 (C.C.P.A. 1970); *see also In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993). To be enabled, all the law requires is that the scope of enablement provided by the specification bear a "reasonable correlation" to the scope of the claims. *Id.* Moreover, even if evidence to doubt the proposed correlation exists, "the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition." *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). Thus, to support a non-enablement rejection, the Examiner must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate the teaching in the specification across the entire scope of the claims. *Id.*

In addition, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A. 1971); MPEP § 2164.02. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.*

THE CLAIMS ARE FULLY ENABLED BY THE INSTANT SPECIFICATION

In light of the legal standard discussed *supra*, applicant submits that the claims, as amended, are enabled by the instant specification. The instant application provides sufficient teaching to enable one of skill in the art to make and use the methods of the invention which involve administering a composition comprising a *Quillaja saponaria* saponin to treat cancer, without undue experimentation, as described below.

The specification provides working examples demonstrating that a composition comprising substantially purified saponin, QS-21, in the absence of a vaccine antigen, and with or without an oligonucleotide containing at least one unmethylated CpG dinucleotide ("CpG oligo"), can stimulate innate immunity (*see* specification at p.32, line 19, to end of p.37, Examples 1, 3 and 5, respectively). The specification also teaches that innate immunity plays an important role in the protective response to cancer, and agents that safely stimulate innate immunity can be used as therapeutic agents against cancer (*see* specification at p.3, lines 15-16, and p.23, lines 15-16). The specification further provides examples of cancers that can be treated by the methods of the present invention (*see* specification at p.23, line 15, to p.24, line 40). Thus, the instant specification fully enables a skilled artisan to use saponin as means of treatment of cancer.

The Examiner's attention is also invited to the Kensil Declaration, which presents *in vivo* data that support the efficacy of the use of saponin for treatment of cancer.

As described therein, substantially purified saponin, QS-21, in the absence of a vaccine antigen, when directly injected into Meth A fibrosarcoma allografts, inhibits the tumor growth (see Paragraphs 5-7 of the Kensil Declaration and Exhibits A-B). The Examiner's attention is further invited to Paragraphs 8-11 of the Kensil Declaration, which present experimental results demonstrating the efficacy of QS-21 against mastocytoma in a mouse P815 tumor model. In the experiments described in Paragraphs 8-11 of the Kensil Declaration, the animal group that received 15 $\mu$ g QS-21 (two days prior to the tumor



transplant, two days after the tumor transplant, and then three times per week afterwards) in the vicinity of the tumor demonstrated lower tumor burden (see Paragraph 9 and Exhibit C) and less tumor occurrence (see Paragraph 10 and Exhibit D). Thus, QS-21 is highly protective against the tumor. These results directly support the teachings of the specification by showing that QS-21, which is effective in stimulating innate immune response, is effective in treating cancer.

In conclusion, the experiments presented in the Kensil Declaration demonstrate that one of skill in the art can readily follow the teachings of the specification to use *Quillaja saponaria* saponin to stimulate innate immunity, and thereby treat cancer, without the need for undue experimentation. In view of the results presented in the Kensil Declaration submitted herewith, Applicant asserts that the claimed methods are enabled. Thus, the rejection under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement should be withdrawn.

### CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application. Claims 31, 33-38, 40 and 44 fully meet all statutory requirements for patentability. Withdrawal of the Examiner's rejections and early allowance and action for issuance are respectfully requested.

Applicant respectfully requests that the Examiner call the undersigned attorney at (212) 790-9090 if any questions or issues remain.

Respectfully submitted,

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Adriane M. Antler 32,605  
Adriane M. Antler (Reg. No.)

**PENNIE & EDMONDS LLP**  
1155 Avenue of the Americas  
New York, New York 10036-2711  
(212) 790-9090

Enclosures